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TECHNOLOGY OF ORGANIC MATTER, POLYMER, AND COMPOSITE MATERIALS

Liquid-Phase Catalytic Oxidation of *p*-Acyl-Substituted Toluenes with Oxygen

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Abstract—A method based on the liquid-phase oxidation of *p*-acyl-substituted toluenes has been developed for the synthesis of *p*-acyl-substituted benzoic acids. It is possible s to recycle the unreacted substrate in this process and to isolate terephthalic acid, which is the second reaction product. A formal kinetic scheme is suggested for the process, which indicates that the reaction products form successively.

Keywords: liquid-phase oxidation, *p*-acyltoluenes, *p*-acylbenzoic acid, kinetics

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Acyl-substituted aromatic carboxylic acids are promising semiproducts of organic synthesis [1–3] for obtaining potentially biologically active compounds. The reactions affording these compounds include the selective oxidation of the methyl group in acyl-substituted toluenes with oxygen in the presence of variable-valence metal ions. There are data concerning the oxidation of *p*-methylacetophenone into *p*-acetylbenzoic acid in the presence of a cobalt–bromide catalyst [4]. Data on the oxidation of other *p*-acyl-substituted toluenes are lacking.

Here, we report the selective oxidation of the methyl group in *p*-acyltoluenes (Fig. 1) and the catalyst composition effect on the selectivity and product yields.

Oxidation was carried out in acetic acid at 95°C [4, 5] in the presence of three different catalytic systems. Cyclohexyl(4-tolyl)methanone (CHTM, **1a**) was chosen to be the model for investigating the oxidation of ketones with the general formula 1 (Fig. 1).

In the oxidation in the presence of the cobalt–bromide catalyst, the main reaction product is 4-(cyclohexylcarbonyl)benzoic acid (CHCBA, **2a**). Terephthalic acid (TPA) forms along with the target product, and its concentration increases during the reaction. The substrate conversion and product accumulation kinetics is illustrated in Fig. 2.

TFA formed a precipitate at the end of the reaction and was separated from the reaction mixture by filtration. CHCBA remained in the solution and was separated by dilution of the filtrate with water followed by filtration of the resulting precipitate. This precipitate was a mixture of CHCBA and unreacted CHTM, which were easily separated by reprecipitation in the form of sodium salts. The substrate thus isolated was then recycled. The characteristics of the resulting CHCBA are presented in the EXPERIMENTAL section.

It seemed pertinent to determine the substrate conversion maximizing the yield, of the target product. It was demonstrated that, at 50% conversion, the yield of the target product (CHCBA) is 84% and the TPA yield is 12% on the reacted substrate basis. Obviously, TPA is a practically important product as well.

As the reaction time is extended, the CHCBA selectivity decreases (Fig. 2). This may be due to CHCBA oxidation to TPA; that is, the following consecutive reactions may take place in the process:

$$\text{CHTM} \xrightarrow{k_1} \text{CHCBA} \xrightarrow{k_2} \text{TPA}.$$

The linearity of the time dependence of the substrate concentration in the *t*–ln[CHTM] coordinates (Fig. 3) is evidence that the reaction is first-order with respect to the substrate.

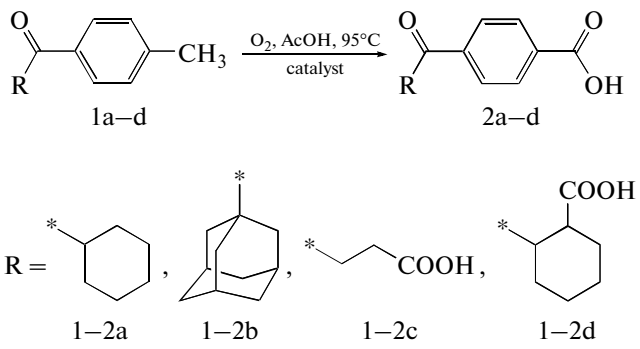

Fig. 1. Catalysts: (I) $Co(OAc)_2 \cdot 4H_2O$, NaBr; (II) $Co(OAc)_2 \cdot 4H_2O$, acetaldehyde; (III) $Co(OAc)_2 \cdot 4H_2O$, $Mn(OAc)_2 \cdot 4H_2O$, NaBr.

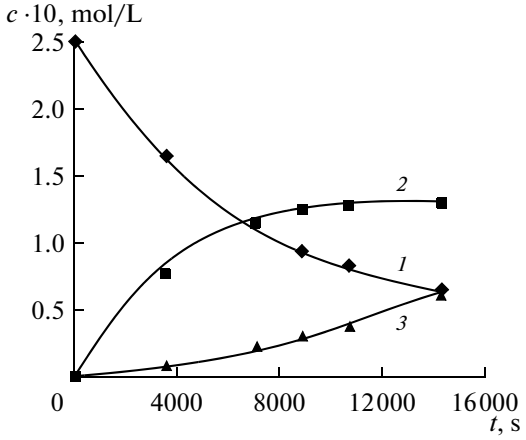

Fig. 2. Substrate conversion and product accumulation kinetics for cyclohexyl(4-tolyl)methanone oxidation: (*1*) cyclohexyl(4-tolyl)methanone (1a), (*2*) 4-(cyclohexylcarbonyl)benzoic acid (2a), and (*3*) terephthalic acid. $[CHTM]_0 = 0.25$ mol/L, $[Co^{+2}]_0 = 3.5 \times 10^{-2}$ mol/L, $[Br^{-1}]_0 = 3.5 \times 10^{-2}$ mol/L, 95°C.

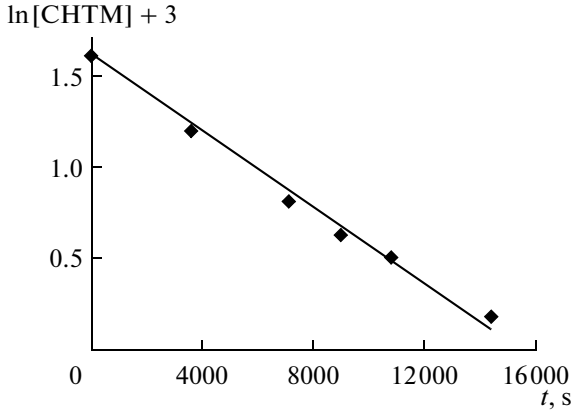

Fig. 3. $[CHTM]_0 = 0.25$ mol/L, $[Co^{+2}]_0 = 3.5 \times 10^{-2}$ mol/L, $[Br^{-1}]_0 = 3.5 \times 10^{-2}$ mol/L, 95°C.

Accordingly, the system of differential equations that mathematically describes the CHTM oxidation reactions appears as

$$\frac{d[CHTM]}{dt} = -k_1[CHTM],$$

$$\frac{d[CHCBA]}{dt} = k_1[CHTM] - k_2[CHCBA],$$

$$\frac{d[TPA]}{dt} = k_2[CHCBA].$$

Solving this system with k_1 and k_2 optimization by least squares led to the following values of the rate constants: $k_1 = (1.7 \pm 0.1) \times 10^{-4}$ s^{-1} and $k_2 = (6.3 \pm 0.9) \times 10^{-5}$ s^{-1}. As follows from these k_1 and k_2 data, the first stage of oxidation in the presence of the cobalt–bromide catalyst is 2.7 times more rapid than the second stage.

A comparison between the oxidation rates of ketone 1a in the presence of different catalytic systems demonstrated that 50% substrate conversion is reached in 1 h with system I (Fig. 1) and in 5 h with system II. Therefore, in the presence of the acetaldehyde initiator, the reaction proceeds much less rapidly. With the cobalt–manganese–bromide catalyst (system III), the dominant reaction product is TPA.

It can be concluded that the process catalyzed by the cobalt–bromide catalyst is more efficient toward the synthesis of CHCBA (**2a**). The process should be conducted at a substrate conversion no higher than 50% with recycling the unreacted substrate. The CHCBA and TPA yields in this case will be 84 and 12%, respectively, on the reacted substrate basis. We developed a process scheme demonstrating that the unreacted substrate can be recycled and the second reaction product—TPA—can be separated.

Substrates 1b, 1c, and 1d (Fig. 1) were oxidized under the same conditions as the model compounds. The reaction was carried out in the presence of the cobalt–bromide catalyst. The concentration of the compounds being oxidized was limited by their solubility. In all of the three cases, at 50% substrate conversion the yield of the main oxidation product was about 70% and the TPA yield was about 15% on the reacted substrate basis. Individual product isolation methods were developed in each particular case. The structures of compounds 2b–2d were identified by ^{1}H NMR spectroscopy.

EXPERIMENTAL

The structures of all synthesized products were confirmed by ^{1}H NMR spectroscopy (Bruker MSL-300 spectrometer operating at 300 MHz, DMSO-*d*6 solvent, tetramethylsilane standard) and IR spectroscopy (Spectrum RX1 instrument).

4-(Cyclohexylcarbonyl)benzoic Acid (2a)

For the oxidation of 1a, 1.51 g (7.5 mmol) of the substrate, 28.0 cm^3 of glacial acetic acid, 0.108 g (1.0 mmol) of sodium bromide, and 0.261 g (1.0 mmol) of cobalt(II) acetate were placed in a four-neck flask fitted with a thermometer, a stirrer, and a backflow condenser. The mixture was heated to 95°C, and oxygen was fed into the flask under stirring. After the completion of the process, the reaction mass was cooled to room temperature. The TPA that precipitated during the reaction was filtered out, and the filtrate was diluted with 100 cm^3 of water. the resulting crystalline precipitate was collected on a filter. The oxidation product was purified from the unreacted substrate by converting it into sodium salts followed by boiling in hydrochloric acid. This yielded 0.8 g of 2a (79% on the reacted substrate basis). M.p. 181–183°C. ^{1}H NMR,

δ, ppm: 13.13 (s, 1H), 8.10–7.95 (m, 4H), 3.38 (t, 1H, $J = 9.0$ Hz), 1.82–1.85 (m, 5H), 1.50–1.15 (m, 5H).

4-(1-Adamantylcarbonyl)benzoic Acid (2b)

Yield: 70%. M.p. 135–140°C, IR, ν, cm^{-1}: 2668 (ν, O–H), 1682 (ν, C=O), 1605 (ν, C=C), 957 (δ, O–H).

4-(3-Carboxypropionyl)benzoic Acid (2c)

Yield: 75%. M.p. 243–245°C. ^{1}H NMR, δ, ppm: 2.64 (t, 2H, $J = 6.2$ Hz), 3.32 (t, 2H, $J = 6.2$ Hz), 8.08 (s, 4H), 13.23 (br s, 2H).

2-(4-Carboxybenzoyl)-1-Cyclohexanecarboxylic Acid (2d)

Yield: 70%. M.p. 194–196°C. ^{1}H NMR, δ, ppm: 1.25 (m, 1H), 1.38 (m, 1H), 1.59 (m, 1H), 1.8 (m, 3H), 2.04 (m, 2H), 2.74 (td, 1H, $J = 9.0, 4.5$ Hz), 3.9 (dd, 1H, $J = 9.0, 4.9$ Hz), 7.96 (d, 2H, $J = 8.0$ Hz), 8.00 (d, 2H, $J = 8.0$ Hz), 12.6 (br s, 2H).

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